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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA AB; AKTIEBOLAGET HÄSSLE; ASTRAZENECA LP; KBI INC.; and KBI-E INC., Plaintiffs and Counterclaim-Defendants, v. HANMI USA, INC., HANMI PHARMACEUTICAL CO., LTD., HANMI FINE CHEMICAL CO., LTD, and HANMI HOLDINGS CO., LTD., Defendants and Counterclaim-Plaintiffs.	Civil Action No. 3:11-CV-00760-JAP-TJB Judge Joel A. Pisano Magistrate Judge Tonianne J. Bongiovanni

ASTRAZENECA'S OPENING *MARKMAN* BRIEF

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I. Introduction

AstraZeneca[1] submits this opening brief in support of its proposed constructions of disputed claim terms in AstraZeneca's U.S. Patent Nos. 5,714,504 ("the '504 patent"; Chen Exh. 1) and 5,877,192 ("the '192 patent"; Chen Exh. 2).[2]

This is a Hatch-Waxman patent infringement action. Hanmi[3] submitted an application to the U.S. Food and Drug Administration ("FDA") seeking approval to market a generic version of AstraZeneca's Nexium® esomeprazole magnesium product prior to the expiration date of the '504 and '192 patents. *See* D.I. 1, 7. Hanmi's proposed generic product, like Nexium®, is an alkaline salt of esomeprazole. Hanmi uses strontium in place of magnesium in its alkaline esomeprazole salt. D.I. 7, 90-2, 113. Nexium® is used, and, if approved, Hanmi's proposed product will be used, to treat gastrointestinal disorders.

The '504 and '192 patents cover pharmaceutical compositions containing alkaline salts of esomeprazole and methods of use thereof. Construction of certain terms in the claims of these patents, whose meaning is disputed, is necessary to resolution of infringement and validity issues in this case.

This Court previously construed certain terms in the '504 and '192 patents. *See AstraZeneca AB v. Dr. Reddy's Labs., Ltd.*, 2010 WL 1981790 (D.N.J. May 18, 2010) (Pisano, J.).

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1 "AstraZeneca" refers collectively to plaintiffs AstraZeneca AB, Aktiebolaget Hässle, AstraZeneca LP, KBI Inc. and KBI-E Inc.

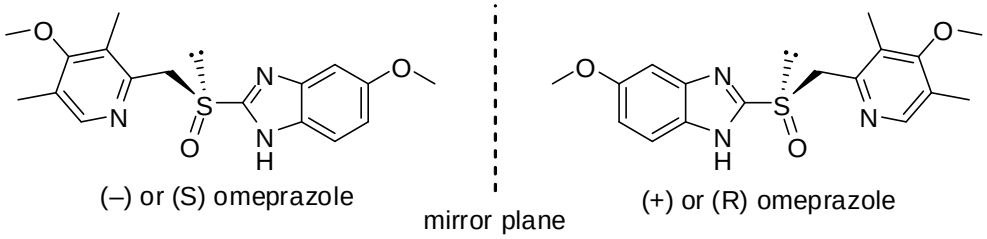
2 Submitted herewith are the Declarations of Patrick L. Chen ("Chen"), Dr. Stephen G. Davies ("Davies") and Dr. David Johnson ("Johnson").

3 "Hanmi" refers collectively to defendants Hanmi, Inc., Hanmi Pharmaceutical Co., Ltd., Hanmi Fine Chemical Co., Ltd. and Hanmi Holdings Co., Ltd.

II. Background

Omeprazole, discovered by AstraZeneca, is a drug known as a proton pump inhibitor ("PPI"). The proton pump is an enzyme, located in the parietal cells that line the stomach, that plays a role in gastric acid production.

Omeprazole is a "racemic mixture" or "racemate," which means that it consists of a 50:50 mixture of two compounds called "enantiomers." Enantiomers are mirror images of each other, much like our hands are mirror images of each other. The two enantiomers—the "(–)" or "*S*" enantiomer and the "(+)" or "*R*" enantiomer—are shown below. The (–) or S enantiomer of omeprazole is known as "esomeprazole." Davies ¶¶ 11, 21–24.



Although successful in treating a number of gastric-acid-related diseases, omeprazole exhibited substantial interindividual variation in therapeutic efficacy. Scientists at AstraZeneca discovered that alkaline salts of esomeprazole provided improved efficacy and decreased interindividual variation; the esomeprazole magnesium in Nexium® is an alkaline salt of esomeprazole. The '504 and '192 patents protect these inventions.

The asserted claims of the '504 patent (claims 1–7 and 10) are directed to "pharmaceutical formulation[s]" containing an "alkaline salt" of esomeprazole and methods of use thereof for "inhibiting gastric acid secretion" and "treatment of gastrointestinal inflammatory

disease."[4] The asserted claims of the '192 patent (1–7, 10–19 and 21–23) are directed to methods for the "treatment of gastric acid related diseases" with esomeprazole "or a pharmaceutically acceptable salt thereof" and to methods for the "production of a medicament for treating gastric acid related diseases" containing the same.

In February 2001, AstraZeneca obtained FDA approval to market Nexium® esomeprazole magnesium. Today, Nexium® is the gold standard in PPI therapy.

III. Claim Construction Principles

The claims of a patent define the scope of the invention and the patentee's rights. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970–71, 980 (Fed. Cir. 1995), *aff'd* 517 U.S. 370, 373–74 (1996). Courts construe claims as "necessary to resolve disputes about claim terms and to assign a fixed, unambiguous, legally operative meaning to the claim." *Liquid Dynamics Corp. v. Vaughan Co., Inc.*, 355 F.3d 1361, 1367 (Fed. Cir. 2004). This determination is made from the perspective of the hypothetical person of ordinary skill in the art in question ("person of ordinary skill") as of the effective filing date of the patent application, and is an issue of law for the court to decide. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (*en banc*); *Markman*, 517 U.S. at 384, 390.

A. Ordinary Meaning in the Context of the Claims

When construing claims, the "analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point out and distinctly claim the subject matter which the patentee regards as his invention.'" *Interactive Gift Exp., Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001) (quoting 35 U.S.C. § 112, ¶ 2, textual modifications adopted); *Phillips*, 415 F.3d at 1312. Thus, claim construction begins with a determination of the "ordinary and customary meaning [a] term

[4] Pending before the Court is AstraZeneca's motion to amend its statement of asserted claims to include claims 3, 5 and 10. *See* D.I. 81, 82, 86, 90. For completeness, AstraZeneca will include these claims in the present claim construction briefing.

would have" to a person of ordinary skill, "in the context of the particular claim in which the disputed term appears." *Phillips*, 415 F.3d at 1312–13 (citations omitted). Extrinsic evidence may be consulted to ascertain the ordinary meaning, *id.* at 1317–19 (see below), but when "the ordinary meaning of claim language as understood by a person of skill in the art [is] readily apparent even to lay judges," claim construction "involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

B. Intrinsic Evidence

Claim terms must also be viewed in the context of the intrinsic evidence—including other claims, the rest of the patent specification and the prosecution history (the back and forth communications between the patent applicant and the U.S. Patent and Trademark Office ("Patent Office")). *Id.* at 1313; *Markman*, 52 F.3d at 980.

Other claims of the patent in question, both asserted and unasserted, can be "valuable sources of enlightenment." *Phillips*, 415 F.3d at 1314. Because claim terms are "normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Moreover, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id*. at 1314–15; *RF Delaware. v. Pac. Keystone Techs.*, 326 F.3d 1255, 1263 (Fed. Cir. 2003).

The rest of the patent specification should also be considered; it can be "the single best guide to the meaning of a disputed claim term," due to its statutory role to "describe the claimed invention in 'full, clear, concise, and exact terms.'" *Phillips*, 415 F.3d at 1315, 1316 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) and 35 U.S.C. § 112 ¶ 1). However, absent "words or expressions of manifest exclusion or restriction," claims should not be restricted to embodiments disclosed in the specification. *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1327, 1328 (Fed. Cir. 2002); *Phillips*, 415 F.3d at 1323 ("Although the specification often describes very specific embodiments of the invention, [the

Federal Circuit has] repeatedly warned against confining the claims to those embodiments.") (citations omitted).

The prosecution history can also be useful in determining the meaning of a claim term, as it provides evidence of "how the [Patent Office] and the inventor understood the patent," and whether a term was "limited" or "explained" during prosecution. *Phillips*, 415 F.3d at 1317; *Markman*, 52 F.3d at 980. However, claims are not limited by the prosecution history unless there is a clear and unambiguous disclaimer of subject matter. *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003); *Markman*, 52 F.3d at 980.

In the absence of contravening intrinsic evidence, the ordinary and customary meaning of a claim term controls. *DSW, Inc. v. Shoe Pavilion, Inc.*, 537 F.3d 1342, 1347 (Fed. Cir. 2008).

C. Extrinsic Evidence

A court also may consider extrinsic evidence, which is "all evidence external to the patent and prosecution history." *Markman*, 52 F.3d at 980. Common forms of extrinsic evidence include expert testimony, technical articles and treatises, and dictionaries. *Phillips*, 415 F.3d at 1317–19. These may be helpful to "establish that a particular term in the patent . . . has a particular meaning in the pertinent field," to "explain how an invention works" or to "provide background on the technology at issue." *Id.*; *Markman*, 52 F.3d at 980. Extrinsic evidence, however, is generally "less reliable than the patent and its prosecution history in determining how to read claim terms," and thus may not be "used to contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Phillips*, 415 F.3d at 1319, 1324; *Markman*, 52 F.3d at 980.

* * *

During claim construction, "[t]he sequence of steps used by the judge in consulting various sources is not important; what matters is for the court to attach the appropriate weight to be assigned to those sources." *Phillips*, 415 F.3d at 1324. Importantly, in this process,

claim terms need be construed "only to the extent necessary to resolve the controversy." *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). Thus, if the ordinary meaning of a term is "readily apparent," the Court may simply rule that the term should carry its ordinary and customary meaning and *not be limited* in a particular manner proposed by a party. *See, e.g., Columbia Sportswear N. Am., Inc. v. Cerf Bros. Bag Co.*, 2007 WL 1792304, *7, 9–11 (D. Or. 2007) (declining to adopt accused infringer's proposed constructions, stating: "this court will not issue an advisory opinion by undertaking to construe the claim terms with greater specificity than necessary to resolve the instant dispute"); *Harris Corp. v. IXYS Corp.*, 114 F.3d 1149, 1152 (Fed. Cir. 1997) (Where a proposed construction would "contribute nothing but meaningless verbiage to the definition of the claimed invention," the term need not be construed.). Relatedly, a Court may decline to entertain a proposed construction that is "so convoluted and artificial" that it "is simply unhelpful" to the claim construction process, *Dayco Prods., Inc. v. Total Containment, Inc.*, 258 F.3d 1317, 1324 (Fed. Cir. 2001), because construction must be "firmly anchored in reality." *Emerson Elec. Co. v. Spartan Tool, LLC*, 223 F.Supp.2d 856, 870–71 (N.D.Ohio 2002) ("claim construction is not philosophy; we need not wring our hands when considering the implications of a metaphysical analysis of claim terms. Instead, we need only recognize that claim construction is firmly anchored in reality[.]") (citation omitted).

IV. Construction of the Disputed Claim Language

Each disputed claim term is addressed in turn below. AstraZeneca's proposed constructions are consistent with the ordinary meaning of the claim language and the intrinsic evidence. Hanmi's proposed constructions are not.

A. ’504 Patent Claim Language

1. “Alkaline salt” (claims 1, 2, 4, 6 and 7)

AstraZeneca’s Proposed Construction	Hanmi’s Proposed Construction
a basic salt (here, a salt in which (–)-omeprazole is negatively charged) that is suitable for use in a pharmaceutical formulation	*Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt*

The term “alkaline salt” appears expressly in ’504 patent independent claims 1, 6 and 7 as part of the phrase “alkaline salt of [esomeprazole],” and, by dependence, in dependent claims 2 and 4. The Court did not construe “alkaline salt” in *Dr. Reddy’s*.

AstraZeneca submits that “alkaline salt” should be given its customary and ordinary meaning. Hanmi asserts, incorrectly, that “alkaline salt” should be limited to the few salts identified in the specification of the ’504 patent as examples of “alkaline” salts.

a. Ordinary Meaning in the Context of the Claims

The words “salt” and “alkaline salt” have ordinary meanings that are well understood by a person of ordinary skill in the art. In particular, a “salt” is a chemical compound made up of two kinds of “ions”—positively-charged “cations” and negatively-charged “anions.” Common table salt (sodium chloride) is an example of a salt, made up of positively-charged sodium cations and negatively charged chloride anions. Davies ¶ 35.

An “acidic” salt is one that is generated under acidic conditions or that generates an acidic solution when put into water. A “basic” salt (also called an “alkaline” salt) is one that is generated under basic or alkaline conditions or that generates a basic or alkaline solution when put into water.[5] Davies ¶ 36.

[5] In chemistry, the degree of acidity or alkalinity of a solution is reflected by a numerical “pH’ scale. A pH of 7.0 is neutral. Solutions with a pH below 7.0 are acidic, and solutions with a pH above 7.0 are basic (or alkaline). Davies ¶ 36 fn. 1.

In chemistry, the word "alkaline" derives from two different groups of metals that react with water to form basic solutions—the "alkali" metals (which include lithium, sodium, potassium, rubidium, and cesium) and the "alkaline earth" metals (which include beryllium, magnesium, calcium, strontium, barium, and radium). Davies ¶ 36.

Thus, in the context of the '504 patent claims, the ordinary meaning of "alkaline salt" of esomeprazole is a basic salt of esomeprazole; that is, a salt of esomeprazole that is generated under basic or alkaline conditions, or one that generates a basic or alkaline solution when put into water. One of ordinary skill in the art would understand that suitable cations for forming an "alkaline salt" of esomeprazole would include, at least, the alkaline metals and alkaline earth metals. One skilled in the art also would understand that such suitable cations also would include an ammonium group,[6] which is an honorary alkaline salt, since ammonia, when dissolved in water, forms a basic or alkaline solution. Davies ¶¶ 36, 37.

For a salt of esomeprazole to be basic, esomeprazole must be anionic (negatively charged) in the salt, and not cationic (in which esomeprazole would be positively charged and acidic), which excludes acid addition salts. Davies ¶¶ 37–40.

In addition, the claims are drawn to a "pharmaceutical formulation" comprising an "alkaline salt" of esomeprazole or methods of use thereof. Thus, the term "pharmaceutical formulation" would be understood to limit "alkaline salts" to those salts suitable for use in pharmaceutical formulations. Davies ¶ 41.

b. Intrinsic Evidence

The specification and prosecution history of the '504 patent both support AstraZeneca's proposed construction of "alkaline salt."

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[6] The chemical group designated "$N^{+}(R)_4$" in the '504 patent is an ammonium group. Davies ¶ 41 fn. 2.

For example, in the '504 patent specification, (i) the "most preferred" salts depicted in structures **I** and **II** in column 3 are individual enantiomers of omeprazole with a negative charge; (ii) the general description of the salt formation specifies that esomeprazole is treated "with a base," rendering it negatively charged, col. 4, ll. 51–61; (iii) Examples 1–3, 6 and 7, in which salts of esomeprazole are initially formed, involve deprotonation of neutral esomeprazole with a base affording it a negative charge; (iv) all exemplary counterions mentioned throughout the specification are positively charged, meaning esomeprazole must bear a negative charge in salts with such counterions; and (v) the specification emphasizes "the surprising high stability in alkaline conditions for the compounds of the invention," as contrasted to the "acidic conditions" employed in unsuccessful prior efforts to prepare "optically pure [individual enantiomers of] omeprazole," *compare* col. 13, l. 31 – col. 14, l. 4 (discussing the stability under alkaline conditions), to col. 1, ll. 27–42 (noting that acidic conditions "would be devastating" for the individual enantiomers of the invention). In addition, the specification discusses the pharmaceutical uses for the invention throughout, supporting the understanding that the claimed "alkaline salts" of esomeprazole are suitable for use in a pharmaceutical formulation. Davies ¶¶ 44–51.

Hanmi's proposal to limit the scope of "alkaline salt" to those specific salts exemplified in the specification ("Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$"), is inconsistent with the claims and specification of the '504 patent. In fact, dependent claims 3 and 10 are limited to the specific "alkaline salts" that Hanmi would have independent claims 1, 6 and 7 limited to. Therefore, under the doctrine of claim differentiation, these independent claims presumptively should not be limited as Hanmi proposes. *Phillips*, 415 F.3d at 1314–15; *RF Delaware.*, 326

F.3d at 1263. The specification also confirms that the salt forms in claims 3 and 10 are merely examples:

> Alkaline salts of the single enantiomers of the invention are, as mentioned above, beside the sodium salts (compounds Ia and Ib) and the magnesium salts (compounds IIa and IIb), ***exemplified by*** their salts with Li^+, K^+, Ca^{2+} and $N^+(R)_4$[.]

Col. 5, ll. 7–11 (emphasis added); Davies ¶¶ 53–54. There are no words or expressions of manifest exclusion or restriction to justify Hanmi's effort to import limitations from the specification into the claims. *Teleflex*, 299 F.3d at 1327, 1328; *Phillips*, 415 F.3d at 1323

Hanmi has cited to various events during the prosecution of the '504 patent in an effort to support its improperly narrow proposed construction. For example, Hanmi cites to a January 21, 1997 Examiner Interview Summary addressing the patentability of claims, in which the Examiner stated:

> A pharmaceutical formulation for oral administration of pure solid state (–) enantiomer of omeprazole Na-salt may be allowable after reviewing the data in affidavit form. . . . The scope of the claim will depend on the data submitted.

Chen Exh. 3. Subsequent events during prosecution, however, demonstrate that Hanmi's proposed construction is *not* suggested by the prosecution history. In a February 18, 1997 response and amendment, the Applicants discussed and submitted a declaration disclosing:

> clinical studies which involved both the monovalent sodium salt and the divalent magnesium salt of the (–)-enantiomer of omeprazole, ***thus supporting the full scope of the genus of alkaline salts disclosed in the application and as claimed herein, as suggested by the Examiner at the interview***.

Chen Exh. 4 at 5 (emphasis added). The claims subsequently allowed are the same claims that ultimately issued. Thus, contrary to Hanmi's argument, the Examiner concluded that the data submitted by the Applicants was sufficient to support the full scope of claims to "alkaline salts."

* * *

The intrinsic evidence reinforces the ordinary and customary meaning of "alkaline salt," and thus no additional extrinsic evidence need be consulted. Properly construed, the claim language "alkaline salt" means *a basic salt (here, a salt in which (–)-omeprazole is negatively charged)*, which covers salts suitable for use in a pharmaceutical formulation and is not limited to the exemplary salt forms in the specification.

2. "(–)-Enantiomer of 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" alone (claims 1, 3–7 and 10) and as modified by "optically pure" (claim 2)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
(–)-omeprazole in at least 94% enantiomeric excess – and when modified by "optically pure" – *in at least 98% enantiomeric excess*	*(–)-omeprazole* or *(–)-enantiomer of omeprazole* – and when modified by "optically pure" – *essentially free of (+)-omeprazole alkaline salt, i.e., the single enantiomer*

The term "(–)-enantiomer of 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" appears in '504 patent independent claims 1, 6 and 7, and, by dependence, in the remaining asserted claims. In claim 2, this term is modified by "optically pure." The Court previously construed these terms in *Dr. Reddy's*, 2010 WL 1981790, at *6–8, to mean *(–)-omeprazole in at least 94% enantiomeric excess*[7] and, when modified by "optically pure," *in at least 98% enantiomeric excess*. In doing so, the Court rejected arguments now advanced by Hanmi here. *Id*. The Court's previous constructions were

[7] The ratio of enantiomers in a mixture is sometimes generally referred to as its "optical purity." "Enantiomeric excess" (e.e.), is one way to quantify optical purity, and reflects the difference between the percentages of the major and minor enantiomers in a mixture. For example, 94% enantiomeric excess (–)-omeprazole means that the ratio of major to minor enantiomers in the mixture is 97:3 (an excess of 94% of (–) relative to (+)). Davies ¶ 30.

correct. AstraZeneca respectfully requests that the Court adopt those constructions here, for the reasons set forth in *Dr. Reddy's*.

3. "Administration of" (claim 6) and "administration to" (claim 7)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
No construction is necessary for these terms; their ordinary and customary meaning would be clear to one skilled in the art. Should construction be undertaken, these terms should be construed to mean: *delivery by any suitable means, including but not limited to ingestion, which may include the prescription by a physician or other licensed healthcare professional, dispensing and ingestion*	*the prescription by a physician or other licensed healthcare professional, dispensing and ingestion*

The term "administration of" appears in asserted claim 6 of the '504 patent and "administration to" appears in asserted claim 7. The Court did not construe these terms in *Dr. Reddy's*.

The dispute over "administration [of/to]" concerns whether its meaning should be limited in the manner proposed by Hanmi: "prescription by a physician or other licensed healthcare professional, dispensing and ingestion;" or should be given its ordinary and customary meaning as proposed by AstraZeneca.

a. Ordinary Meaning in the Context of the Claims

The Court need not consult a dictionary or an expert in order to determine that "administration," *e.g.*, of a medicine, *does not require* "prescription by a physician or other licensed healthcare professional, dispensing and ingestion." While it is true that drugs are often prescribed by a physician and dispensed by a pharmacist, many drugs may be obtained over-the-counter and administered without a prescription or involvement of any "licensed healthcare professional." Omeprazole magnesium (in Prilosec® OTC) is one such example. Johnson ¶¶

24, 26. Hanmi's proposed construction is not found anywhere in the intrinsic evidence and it is "convoluted and artificial" and not "firmly anchored in reality," and therefore should be dismissed. *Dayco Prods.*, 258 F.3d at 1324; *Emerson Elec.*, 223 F.Supp.2d at 870–71.

Moreover, in the claims, these terms are always modified by "oral," from which a person of ordinary skill would understand that "administration" refers to the means of delivery of the medicine (*i.e.*, by mouth), rather than to "the prescription by a physician or other licensed healthcare professional, dispensing and ingestion," modification of which by "oral" would be nonsensical. Johnson ¶¶ 29, 32.

Thus, based just on the ordinary meaning of these terms as used in the claims in which they appear, the Court should decline to adopt Hanmi's proposed construction.

b. Intrinsic Evidence

Hanmi's proposed construction is also inconsistent with the intrinsic evidence. The specification explains that the compounds of the invention are "formulated into pharmaceutical formulations for oral, rectal, parenteral or other modes of administrations." Col. 5, ll. 12–15. From this context, and the subsequent elaboration of exemplary formulations for "oral administration," "rectal administration" and "parenteral administration", and the reference to the "route of administration" in the context of discussing dosage, it is evident that "administration" in the '504 patent is often used to convey the means by which the compositions of the invention may be delivered. Col. 5, l. 25 – col. 6, l. 24; col. 12, ll. 43–54. Nowhere is the specification limited to an "administration" *requiring* a prescription or the involvement of any "licensed healthcare professional." Although a licensed healthcare professional or physician is required to diagnose and prescribe a prescription medicine, the specification is not so limited and, as discussed above, such a limitation would be inconsistent with the term's usage in reference to the means of delivery. Johnson ¶¶ 28, 30–32.

Hanmi points to sections in the '504 patent specification containing the term "patient," presumably to bolster its argument that "administration" requires the involvement of a physician. Col. 2, ll. 12–37 and col. 6, ll. 21–25. However, "patient" as used in the '504 patent, describes nothing more than a person with a condition that may benefit from treatment; it does not always or necessarily *require* the participation of a physician. For example, the term "patients" is used in conjunction with "NSAID therapy." Col. 2, ll. 25–26. NSAIDs (non-steroidal anti-inflammatory drugs) include common over-the-counter medications like aspirin, ibuprofen and naproxen, and thus "patients," as used in that portion of the '504 patent, does not *require* the participation of a physician. Johnson ¶¶ 33–35.

* * *

Because the meaning of this term is readily apparent and the specification does not introduce any ambiguity or support Hanmi's narrow construction, no additional extrinsic evidence need be consulted. "Administration [of/to]" should be given its ordinary and customary meaning *and not be limited* in the manner that Hanmi has proposed. *Columbia Sportswear*, 2007 WL 1792304, at *7, 9–11; *Harris*, 114 F.3d at 1152. Should the Court wish to provide a construction that reflects the ordinary meaning, AstraZeneca has proposed a construction that is consistent with the intrinsic evidence and that (in an effort to compromise) incorporates Hanmi's proposed language: *delivery by any suitable means, including but not limited to ingestion, which may include the prescription by a physician or other licensed healthcare professional, dispensing and ingestion*.

4. "A mammal including man in need of such treatment" (claim 7)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
No construction is necessary for this term; its ordinary and customary meaning would be clear to one skilled in the art. Should construction be undertaken, this term should be construed to mean: *a mammal including man who may obtain a benefit*	*a mammal including man in whom the need for treatment of gastrointestinal inflammatory disease is recognized and/or appreciated by the physician or other licensed healthcare professional*

The term "a mammal including man in need of such treatment" appears in asserted claim 7 of the '504 patent. The Court did not construe this term in *Dr. Reddy's*.

The dispute here concerns whether this language should be limited to the narrow meaning proposed by Hanmi: "a mammal including man in whom the need for treatment of gastrointestinal inflammatory disease is recognized and/or appreciated by the physician or other licensed healthcare professional," or should be given its ordinary and customary meaning as AstraZeneca proposes.

a. Ordinary Meaning in the Context of the Claims

The Court need not consult a dictionary or an expert in order to determine that "a mammal including man in need of such treatment" *does not require* "the need for treatment of gastrointestinal inflammatory disease [to be] recognized and/or appreciated by the physician or other licensed healthcare professional." Generally speaking, while the "need" for a medical treatment may be assessed by a physician, as noted above many drugs may be obtained over-the-counter and administered without a prescription or involvement of any "licensed healthcare professional." Here, a person of ordinary skill in the art would understand the term "man in need of such treatment" to mean a person with a condition, *i.e.*, a class of patient (*e.g.*, persons with a gastrointestinal inflammatory disease); the term does not require recognition or appreciation by anyone, let alone a physician. Johnson ¶¶ 39–41. Hanmi's position is nowhere set forth in the

intrinsic evidence and is yet another "convoluted and artificial" construction not "firmly anchored in reality" that should be dismissed. *Dayco Prods.*, 258 F.3d at 1324; *Emerson Elec.*, 223 F.Supp.2d at 870–71.

b. Intrinsic Evidence

Nowhere does the specification limit claim 7 to *require* recognition or appreciation by a physician or anyone else. Johnson ¶¶ 42, 43.

* * *

Because the meaning of this term is readily apparent and the specification does not introduce any ambiguity or support Hanmi's narrow construction, no additional extrinsic evidence need be consulted. The term "a mammal including man in need of such treatment" should be given its ordinary and customary meaning *and not be limited* in the manner that Hanmi has proposed. Should the Court wish to provide a construction that reflects the ordinary meaning, a reasonable construction would be *a mammal including man who may obtain a benefit*.

B. '192 Patent Claim Language

1. "Pharmaceutically acceptable salt" (claims 1–7, 10–19 and 21–23)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
a basic salt (here, a salt in which (–)-omeprazole is negatively charged) that is suitable for pharmaceutical administration	*Na^+, Mg^{2+}, Li^+, K^+, Ca^{2+} or $N^+(R)_4$ salt* – or – *an acid or alkaline pharmaceutically acceptable nontoxic salt*

The term "pharmaceutically acceptable salt" appears expressly or by dependence in all of the asserted claims of the '192 patent. The Court declined to construe this term in *Dr. Reddy's*, ruling that the ordinary meaning would be understood by a person of ordinary skill. *Dr. Reddy's*, *21. In *Dr. Reddy's*, however, there was no controversy necessitating the construction

of this term with any further specificity. Here, Hanmi's contentions raise issues that were not present in *Dr. Reddy's,* warranting construction of this term.

As with the term "alkaline salt," the parties dispute whether "pharmaceutically acceptable salt" in the '192 patent claims should be limited to the exemplary salts in the specification of the '504 patent, as Hanmi proposes, or should carry the ordinary meaning of "alkaline salt" discussed above, as AstraZeneca proposes. Hanmi has also proposed an alternative construction that would allow the "pharmaceutically acceptable salts" of the invention to cover acid addition salts; a construction with which AstraZeneca disagrees.

a. Ordinary Meaning in the Context of the Claims

A "pharmaceutically acceptable salt" is one suitable for pharmaceutical administration. This ordinary understanding is supported by the fact that these claims are directed to the administration of the claimed salts in pharmaceutical methods of treatment. In the claims of the '192 patent, "pharmaceutically acceptable salt" always modifies the chemical name for esomeprazole. Thus, the claimed salt is a salt of esomeprazole suitable for pharmaceutical administration. Davies ¶¶ 60–62.

b. Intrinsic Evidence

The intrinsic evidence reveals that the meaning of "pharmaceutically acceptable salt" in the '192 patent claims is the same as that for "alkaline salt" in the '504 patent claims.

The '192 patent states at the outset: "The description of salt forms of the single enantiomers of omeprazole and the process of making the same is herein incorporated by reference to copending Ser. No. 08/376,512." Col. 1, ll. 10–13. U.S. Patent Application No. 08/376,512 is the application that issued as the '504 patent. Therefore, for all of the reasons stated above in the context of addressing the meaning of "alkaline salt" in the '504 patent claims, the "salt" of the '192 patent claims would be understood to be a basic salt, that is, one in which

esomeprazole is negatively charged, and not limited to the exemplified salts in the '504 patent specification. Davies ¶ 64. In addition, the use of the salts in pharmaceutical compositions and methods of use in the '504 patent, and in the methods of pharmaceutical administration of the '192 patent, confirm the ordinary understanding that the claimed salts are suitable for pharmaceutical administration.

As for Hanmi's alternative construction of this term—*i.e.*, that it includes acid addition salts of esomeprazole—Hanmi cites to column 4, lines 14–16 of the '192 patent, where it states that "the term 'pharmaceutically acceptable salt' refers to both acid and alkaline pharmaceutically acceptable non-toxic salts." This statement, however, appears in a paragraph that is not limited to esomeprazole as the only active pharmaceutical ingredient, and in fact indicates that "other therapeutic ingredients are especially of interest." Col. 4, ll. 9–19. In the overall content of the '192 patent, a person of ordinary skill thus would not read this statement to say that the salts of esomeprazole could be acid addition salts. Because of its unambiguous reference to the "salt forms of the single enantiomers of omeprazole" as described in the '504 patent (*see* '192 patent at col. 1, ll. 10–13), the '192 patent plainly should be understood to be focused on *alkaline* salts of esomeprazole. Davies ¶¶ 65–66.

Moreover, when addressing the term "alkaline salt," the '504 patent specification emphasizes "the surprising high stability in alkaline conditions for the compounds of the invention," as contrasted to the "acidic conditions" employed in prior art in unsuccessful efforts to prepare "optically pure [individual enantiomers of] omeprazole." Compare col. 13, l. 31 to col. 14, l. 4, to col. 1, ll. 27–42 (noting that acidic conditions "would be devastating" for the individual enantiomers of the invention). This text would confirm the understanding of a person of ordinary skill, that "pharmaceutically acceptable salts" of esomeprazole in the '192 patent are "alkaline salts," just as in the '504 patent, and do not include acid addition salts. Davies ¶ 67.

* * *

The intrinsic evidence thus provides an unambiguous meaning of "pharmaceutically acceptable salt": *a basic salt (here, a salt in which (–)-omeprazole is negatively charged)*, which is suitable for pharmaceutical administration, is not limited to the exemplary salt forms in the specification and does not include acid addition salts. No additional extrinsic evidence need be consulted.

2. "Consisting essentially of the (–)-enantiomer of 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" (claims 1–7, 10–19, 21 and 22)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
(–)-omeprazole in at least 98% enantiomeric excess	*[(–)-omeprazole* or *(–)-enantiomer of omeprazole] that may also contain substances that do not materially affect the claimed novel properties*

The term "consisting essentially of the (–)-enantiomer of 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole" appears expressly or by dependence in asserted claims 1–7, 10–19, 21 and 22 of the '192 patent. The Court previously construed this term in *Dr. Reddy's*, at *9–10, to mean *(–)-omeprazole in at least 98% enantiomeric excess*. The Court's previous construction was correct. AstraZeneca respectfully requests that the Court adopt that construction here, for the reasons set forth in *Dr. Reddy's*.

3. "Administering to a mammal in need of treatment" (claims 1–7, 10, 11 and 23)

AstraZeneca's Proposed Construction	Hanmi's Proposed Construction
No construction is necessary for this term; its ordinary and customary meaning would be clear to one skilled in the art. Should construction be undertaken, this term should be construed to mean: *delivery by any suitable means, including but not limited to ingestion, which may include the prescription by a physician or other licensed healthcare professional, dispensing and ingestion, to a mammal who may obtain a benefit*	*the prescription by a physician or other licensed healthcare professional, dispensing and delivery by any suitable means*

The term "administering to a mammal in need of treatment" appears expressly or by dependence in asserted claims 1–7, 10, 11 and 23 of the '192 patent. The Court did not construe this term in *Dr. Reddy's*.

As with the terms "administration [of/to]" and "a mammal including man in need of such treatment" in the '504 patent claims, sections V.A.3. and 4. *supra*, the parties dispute whether this claim language should be limited to the narrow meaning proposed by Hanmi or should carry its ordinary and customary meaning, as AstraZeneca proposes.

a. Ordinary Meaning in the Context of the Claims

For the same reasons discussed above when addressing the terms "administration [of/to]" and "a mammal including man in need of such treatment" in the '504 patent claims (at sections V.A.3. and 4. *supra*), the Court need not consult a dictionary or an expert in order to rule that Hanmi's construction is unnecessarily narrow and not "firmly anchored in reality." Johnson ¶¶ 46–49.

b. Intrinsic Evidence

Hanmi's proposed construction is also inconsistent with the intrinsic evidence.

The specification reveals that "administering" in the '192 patent, like "administration" in the '504 patent, often refers to the means by which the compounds of the invention may be delivered. For example, claim 7, which depends from "claim 1 or 2" limits the methods to those in which the compounds are "administered orally." Similarly, claim 19, which depends from claim 12, limits the method to those in which the "medicament" is produced for "oral administration." Dependent claims 8, 9 and 20 similarly limit the methods to those in which the compound or "medicament" is "administered parenterally" or "administered by intravenous infusion." The specification goes on to explain that the compounds of the invention are "suitable for oral, rectal or parenteral such as subcutaneous, intramuscular, and intravenous administration." Col. 4, ll. 3–8, 19–21; Johnson ¶¶ 50, 51.

Nowhere do the claims or the specification indicate that a "licensed healthcare professional" *must always* be involved either for assessing "need" of a patient or for "administration," and limiting the claim language in the manner proposed by Hanmi would be inconsistent with the term's usage in reference to the means of delivery. Johnson ¶ 52.

* * *

Because the meaning of this term is readily apparent and the specification does not introduce any ambiguity or support Hanmi's narrow construction, no additional extrinsic evidence need be consulted. The term "administering to a mammal in need of treatment" should be given its ordinary and customary meaning *and not be limited* in the manner that Hanmi has proposed.

Should the Court wish to provide an alternative reflection of the ordinary meaning, AstraZeneca has proposed a construction that is consistent with the ordinary meaning and intrinsic evidence and that (in an effort to compromise) incorporates Hanmi's proposed language: *delivery by any suitable means, including but not limited to ingestion, which may*

include the prescription by a physician or other licensed healthcare professional, dispensing and ingestion, to a mammal who may obtain a benefit.

V. Claim Construction Issues Raised in Hanmi's Summary Judgment Motions

Hanmi has filed five summary judgment motions. D.I. 97–117.

In its "Motion for Summary Judgment No. 3: Invalidity of U.S. Patent No. 5,714,504 – Claims 1-2, 4, 6 and 7 Based on 'Solid State'" ("Motion 3"), Hanmi asserts that the '504 patent claim term "solid state" has no art-recognized meaning. D.I. 101-2 at 8. But, this Court, in *Dr. Reddy's*, determined that "solid state" should be given its customary and ordinary meaning which "would be clear to one skilled in the art." *Dr. Reddy's*, at *9. At a minimum, to the extent Hanmi is now contesting the Court's prior claim construction determination, its Motion 3 will require the parties and the Court to address this *as part of claim construction*.

In its "Motion for Summary Judgment No. 1: Non-Infringement of U.S. Patent No. 5,877,192 – Claims 1-11, 13-18 and 20-23" ("Motion 1"), Hanmi alleges that infringement of claims 1–13, 23–18 and 20–23 of the '192 patent requires "clinical evaluation" of a particular benefit esomeprazole exhibits as compared to omeprazole. D.I. 98 at 3–4. For this theory, Hanmi relies on language in these claims that the Court previously construed, *Dr. Reddy's*, at *10–19, and which construction the parties here agreed to adopt. D.I. 92. AstraZeneca submits that the Court's previous construction does not require any "clinical evaluation," and thus, at a minimum, some clarification of the Court's previous claim construction is necessary to resolve Motion 1.

AstraZeneca will respond to Hanmi's summary judgment motions in due course. But, with respect to Hanmi's Motions 1 and 3, AstraZeneca submits that any claim construction issues presented by those motions logically should be considered at the same time as the other claim construction issues described in this brief. Accordingly, AstraZeneca submits that the schedule of the present *Markman* proceedings be coordinated with any schedule for resolution of

Motions 1 and 3. It makes no sense for the Court to address different claim construction issues on different tracks. What makes sense is to conflate these different schedules into a single schedule.

VI. Conclusion

For the foregoing reasons, AstraZeneca respectfully requests that the Court adopt AstraZeneca's proposed constructions of the claim terms in dispute.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on November 7, 2011, I caused a copy of the foregoing ASTRAZENECA'S OPENING *MARKMAN* BRIEF and supporting documents to be served upon the following counsel by operation of the Court's electronic filing system and/or electronic mail:

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